Cardiogenic Shock: A Lethal Complication of Acute Myocardial Infarction

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Cardiogenic shock is a serious complication of myocardial infarction (MI) that affects approximately 7% of MI patients, accounting for the majority of all deaths related to acute infarction. Shock is typically the result of a massive amount of damage to the left ventricular myocardium; its defining characteristics are hypotension (systolic blood pressure [SBP] of 90 mm Hg or less, or in chronically hypertensive patients a drop in SBP of 30 mm Hg or more) and hypoperfusion. Shock occurs more frequently in ST-segment elevation MI (STEMI) patients than in non-STEMI patients. Revascularization, either with angioplasty or coronary bypass graft surgery, is associated with better outcomes than intensive medical therapy in patients with shock. Adjunctive therapies include vasopressor therapy, mechanical ventilatory support, and intra-aortic balloon pump counterpulsation (IABP). IABP can stabilize some patients and may make revascularization safer. Other adjunctive therapies being investigated include improved mechanical support devices, induction of systemic hypothermia, use of supersaturated oxygen, and, as medical therapy, administration of L-NMMA.

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Key words: Hypotension • Hypoperfusion • Systolic blood pressure • Revascularization • STEMI

The development of cardiogenic shock portends an extremely poor prognosis. An expanding body of knowledge is accumulating on this high-risk group of patients.

Table 1
Baseline Patient Characteristics of ST Elevation Versus Non-ST Elevation Shock Patients

	GUSTO IIB			SHOCK Registry		
	ST Elevation	No ST Elevation	*P*	ST Elevation (n = 729)	No ST Elevation (n = 152)	*P*
Age (y)	70	73	0.015	67.9	71.4	< 0.001
Prior MI (%)	24	44	< 0.001	36.7	55.7	< 0.001
Prior CABG (%)	4	18	< 0.001	8.4	18.5	< 0.001
CHF (%)	4	12	0.001	16.5	35.2	< 0.001
Hx CRI (%)	—	—	—	8.4	20.7	< 0.001
DM (%)	21	34	0.002	33.2	31.3	0.703
PVD (%)	—	—	—	16.4	28.4	0.007

GUSTO, Global Use of Strategies to Open Occluded Coronary Arteries; SHOCK, Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock; MI, myocardial infarction; CABG, coronary artery bypass graft; CHF, congestive heart failure; CRI, cardiac risk index; DM, diabetes mellitus; PVD, peripheral vascular disease.
Reproduced with permission from Holmes and Hasdai.[8]

Defining Cardiogenic Shock

The definition of shock is crucial to evaluating the available data. The definitions are varied, which may account for some of the differences in outcome in previous reports. Hypotension is central to any definition. Although the level of hypotension required to meet this criterion has varied, it is generally a systolic blood pressure (SBP) of 90 mm Hg or less. In patients who have been hypertensive, a drop in SBP of 30 mm Hg or more is often included as meeting the definition of shock. It is apparent that some patients with chronic conditions, such as severe refractory congestive heart failure, may have a resting SBP of approximately 90 mm Hg. This may make the definition of shock in these patients more problematic. In addition to hypotension, hypoperfusion must be present, despite adequate filling pressure. This hypoperfusion may be manifested as cool, poorly perfused extremities, decreased urine output, or acutely diminished central nervous system function.

The concept of "pre-shock" has received recent attention. Pre-shock patients have very marginal hemodynamics and may develop full-blown shock; they may, however, have improved outcome if identified and treated early.

In those patients with non-STEMI, the incidence of shock is approximately 50% of that seen in patients with STEMI.

Incidence

Data on temporal trends in cardiogenic shock have come from several sources, including randomized clinical trials and community- and country-based registries.[1–4] Goldberg and colleagues[3] evaluated such trends in a single community from 1975 to 1997. The overall incidence during this time was 7.1% and ranged over a fairly tight distribution, from 4.5% to 8.6%. In three large, international series of patients with ST-segment elevation myocardial infarction (STEMI) receiving thrombolytic therapy, the incidence of shock has ranged from 4.2% to 7.2%.[2,4,5] Finally, in a multicenter, nationwide study from 27 centers in Denmark, patients with enzyme-confirmed MI were evaluated from 1990 to 1992.[6] Of 6676 consecutive patients, shock occurred in 6.7%. These studies are all reasonably consistent and give a good estimate of the incidence of shock in relatively current practices.

Clinical Setting

The clinical setting of shock varies widely because multiple diseases may present with shock, including (among others) sepsis, pulmonary embolism, blood loss, trauma, and acute valvular heart disease lesions.

In the setting of an acute ischemic event, shock may occur in patients with either non–STEMI or STEMI. In the former group, the incidence of shock is lower, approximately 50% of that seen with STEMI. Those patients with non-STEMI who develop shock have more adverse baseline characteristics, including older age, higher incidence of diabetes, and a higher incidence of prior infarction (Table 1).[8]

Shock may occur in the setting of first infarction if the infarct-related artery supplies the majority of left ventricular myocardium, as might be seen with proximal left anterior descending occlusion or occlusion of the dominant left circumflex coronary artery. It may also occur with inferior infarction if there is right ventricular involvement along with posterior left ventricular myocardial involvement. Shock may also be the result of multiple smaller infarctions that add up to severely compromised left ventricular function.

The timing of shock varies[2,6,9] depending on the data used to assess its onset. In series of patients randomized to thrombolytic therapy, shock may be relatively uncommon early on because those patients with shock may not be randomized. In these trials, shock may develop subsequently as a result of reinfarction or recurrent ischemia. In the TRandolapril Cardiac Evaluation (TRACE) registry,[6] 59% of shock patients developed shock within 48 hours of onset of infarction, but 30% developed it 5 days or more after the index infarction. In other series, only approximately 10% of patients presented with shock on admission.[2,5,8] Patients who develop shock with non–STEMI usually develop it later on during the course of hospitalization than do patients with STEMI.[2,5,8]

Etiology

As previously mentioned, the etiology of cardiogenic shock varies. Although it is typically the result of a massive amount of damage to the left ventricular myocardium, other causes must be ruled out. In the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) registry, predominant left ventricular failure was seen in 74.5% of patients (Figure 1).[10] However, acute severe mitral regurgitation was seen in 8.3%, ventricular septal rupture in 4.6%, and right ventricular shock in 3.4%. Delineation of the specific etiology of shock has obvious importance for selecting an optimal treatment strategy.

Patients with shock account for the majority of all deaths related to acute infarction.

Outcome

Shock has been associated with marked increase in mortality. Indeed, patients with shock account for the majority of all deaths related to acute infarction.[2,3,4] There is, however, community-based data to suggest that the outcome of shock may be improving. Goldberg and colleagues, during a 23-year period, found the greatest improvement in mortality during the last decade (the 1990s).[3] From 1975 through 1990, there was 70% in-hospital mortality, which declined to 61% between 1993 and 1995 and to 59% in 1997. Irrespective of whether shock occurs in the setting of STEMI or non–STEMI, 30-day mortality in thrombolytic trials has been very high, approximately 60% or greater.[5]

Intensive resources are both required and consumed in shock patients.[11] Adjunctive therapy is important, including vasopressor therapy, mechanical ventilatory support, and intra-aortic balloon pump counterpulsation (IABP). It is hard to separate out the independent effect of each of these therapies on outcome, particularly for IABP, because this type of circulatory support is usually combined with revascularization. Clearly, IABP can stabilize some patients and may make revascularization safer.[12–14]

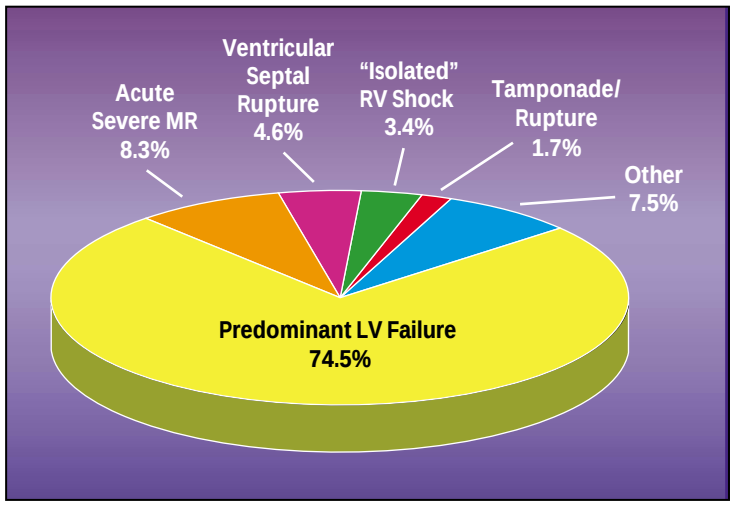

Figure 1. *Baseline characteristics of patients with cardiogenic shock subgrouped into those with STEMI and those with NSTEMI. LV, left ventricular, MR, mitral reflux; RV, right venticular.*

There are data to suggest that this approach is underutilized in managing patients with shock.[14] When an invasive approach with revascularization is considered, an IABP should usually be placed, unless it is contraindicated (eg, in the presence of severe peripheral vascular disease).

Revascularization for shock patients has received considerable scrutiny.[15–18] Multiple small, often single-center, registry experiences documented that revascularization was associated with improved survival.[15] These analyses suffer from the issues of patient selection bias. In a trial involving one of the largest shock populations studied to date (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries, GUSTO-I),[2] those patients who developed shock after arrival, and in whom revascularization was achieved with percutaneous transluminal coronary angioplasty, had a mortality rate of 32%. In those patients undergoing surgical revascularization, mortality was 29%, compared with patients treated with lytic therapy alone, in whom the mortality rate was 75%. In the National Registry of Myocardial Infarction experience, similar results were seen.[12]

Only one randomized trial has been completed—the SHOCK trial.[19] SHOCK randomized patients to either an aggressive, invasive approach with angioplasty or coronary bypass graft surgery, generally with IABP, or to intensive medical therapy, which often included thrombolytic therapy and IABP. In the intensive medical therapy arm, revascularization was permitted if indicated > 54 hours after study entry. The primary endpoint in this trial was 30-day mortality. The 30-day mortality rate in the invasive therapy arm was 46.7%, compared with 56% in the conservative arm (P = .11). At 6 months, however, mortality was significantly lower in the revascularization group, 50.3% compared with 63.1% (P = .027) in the medical therapy group. In a predefined subset analysis, early revascularization benefits were only seen in patients younger than 75 years. In this subset of the revascularization group, 30-day mortality was 41.4% compared with the medical therapy group, in whom 30-day mortality was 56.8%. The results of the SHOCK trial are relatively consistent with the other series in which revascularization is associated with improved outcome.

Longer-term outcome is less promising: at 6 years in the TRACE registry, total cumulative mortality was 88%.

Intermediate-term outcome of shock patients is good.[20,21] In the GUSTO-I trial, of those patients who survived 30 days, 85% were alive at 1 year.[20] Longer-term outcome, however, is less promising: at 6 years in the TRACE registry, total cumulative mortality was 88%.[6]

Adjunctive Therapies

Despite successful revascularization, mortality in patients with cardiogenic shock remains very high. There has been interest in improved mechanical support devices that result in better hemodynamic improvement.[22] These may make revascularization safer. Because they can be used to unload the ventricle, these devices may also enhance myocardial salvage. Systemic hypothermia is being tested in the setting of acute MI without shock. Lowering

Main Points

- Cardiogenic shock accounts for the majority of all deaths related to acute myocardial infarction (MI).
- The defining characteristics of shock are hypotension (systolic blood pressure [SBP] of 90 mm Hg or less, or in primarily hypertensive patients a drop in SBP of 30 mm Hg or more) and hypoperfusion.
- Shock may occur either in ST-segment elevation MI (STEMI) or non-STEMI patients. The incidence of shock in non-STEMI is lower, approximately 50% of that seen with STEMI. Non-STEMI patients who develop shock have more adverse baseline characteristics, including older age, more diabetics, and a higher incidence of prior infarction.
- Revascularization for shock patients has received considerable scrutiny; in the GUSTO-I trial, patients who developed shock in whom revascularization was achieved with percutaneous transluminal coronary angioplasty had a mortality rate of 32%, and in those patients undergoing surgical revascularization mortality was 29%, compared with patients treated with lytic therapy alone, in whom the mortality rate was 75%.
- The SHOCK trial also showed that revascularization is associated with better outcomes than intensive medical therapy in patients with shock.

core temperature to approximately 33°C has been shown in animal models to significantly improve myocardial salvage. Early human data supports this. Such technology may also be very helpful in shock patients. In addition, supersaturated oxygen is being tested.

Adjunctive medical therapies also continue to evolve. N^G-monomethyl-L-arginine (L-NMMA), an antagonist of nitric oxide synthase, has been studied in a small pilot study of 11 patients with persistent cardiogenic shock.[23] All of the patients were on IABP, mechanical ventilation, and large doses of vasopressors. Administration of bolus and infusion of L-NMMA resulted in sustained improvement in arterial pressure and urine output. Ten of the 11 patients could be weaned from mechanical ventilation and IABP, and seven were dismissed home and were alive at a 1–3-month follow up. This approach is currently under evaluation for a large, multicenter, randomized clinical trial.

Summary

Cardiogenic shock remains a lethal event for a substantial number of patients with acute myocardial infarction. Although the incidence has remained stable, mortality appears to be declining as we focus more on early, intensive, aggressive strategies. Even with early revascularization, mortality rates remain high. Newer strategies are required to identify and treat those patients for whom recovery is not only desirable but possible. ■

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